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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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EXAMINER	
NICHOLS, CHRISTOPHER J	

ART UNIT	PAPER NUMBER
1647	

DATE MAILED: 01/31/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/787,126	HALKIER ET AL.	
	Examiner	Art Unit	
	Christopher J Nichols, Ph.D.	1647	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *29 October 2004*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,3,5,8-12,17-24,28 and 57-60* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,3,5,8-12,17-24,28 and 57-60* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☒ Claim(s) *1,3,5,8-12,17-24,28 and 57-60* are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☒ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☒ Interview Summary (PTO-413) Paper No(s)/Mail Date. 1/11/05, 1/31/05, 12/28/04
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Status of Application, Amendments, and/or Claims

1. The Response and Amendment filed 29 October 2004 has been received and entered in full.

2. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Withdrawn Objections And/Or Rejections

3. The Objection to the Specification as set forth in the previous Office Action (29 April 2004) is hereby *withdrawn* in view of Applicant's amendments (29 October 2004).

4. All rejections of the claims as set forth at in the previous Office Action (29 April 2004) are *withdrawn in part* in view of Applicant's amendments and arguments (29 October 2004).

Obvious-Type Non-Statutory Double Patenting

5. Claims **1, 3, 5, 8-12, 17-24, 28,** and **57-60** are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims **1-19** of U.S. Patent No. 6,645,500. Although the conflicting claims are not identical, they are not patentably distinct from each other because both the claims of the instant application and US 6,645,500 encompass a method of administering a modified OPGL polypeptide or analogue comprising a modified OPGL polypeptide and a foreign, promiscuous, immunodominant T_H epitope to down-regulate endogenous OPGL activity in an animal. The instant Applicant claims a broader embodiment of the same method wherein the modified OPGL polypeptide comprising OPGL

with any immunogenic agent including but not limited to foreign, promiscuous, immunodominant T_H epitope. Thus the invention of US '500 is a species of the genus instantly claimed and as such the two sufficiently overlap in scope.

Claim Rejections - 35 USC § 112

6. Claims **1, 3, 5, 8-12, 17-24, 28,** and **57-60** are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for *a method for in vivo down-regulation of osteoprotegerin ligand (OPGL) activity in a mammal, the method comprising effecting presentation to the mammal's immune system of an immunologically effective amount of*

> *at least one modified mammalian OPGL polypeptide or analogue thereof which has a result that immunization of the mammal with the modified mammalian OPGL polypeptide or analogue thereof induces production of antibodies against the mammal's own OPGL polypeptide which down-regulates the mammal's own OPGL activity,*

wherein said modified mammalian OPGL polypeptide or analogue thereof comprising at least residues 158 to 316 of OPGL and is modified by the introduction of immunogenic amino acid sequences which are introduced such that inherent B-cell epitopes in said OPGL polypeptide or analogue are preserved, does not reasonably provide enablement *for other permutations of the claimed formula, substitutions, mutations, insertions, deletions, and other alterations, other animal OPGLs*. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to **make** or **use** the invention commensurate in scope with these claims.

7. The Specification teaches that the growth, development, and maintenance of bone is a highly regulated process balanced between the opposing activity of two cells, osteoblasts (derived from mesenchymal stem cells) which make bone and osteoclasts (derived from hematopoietic precursors of the monocytes-macrophage lineage) which breakdown bone (resorption). The disruption of the harmonious counteraction of osteoblasts and osteoclasts can lead to skeletal abnormalities characterized by either increased bone mass (osteopetrosis) or decreased bone mass (osteoporosis) (pp. 2-3). Osteoprotegerin is a novel secreted member of the tumor necrosis factor receptor family which blocks osteoclastogenesis *in vitro* in a dose dependent manner (pp. 3). Osteoprotegerin ligand (OPGL) binds to osteoprotegerin and osteoclasts. OPGL is a potent activator of mature osteoclasts which leads to an increase in bone resorption (pp. 6 lines 8-20). The amino acid sequence of SEQ ID NO: 2 is human OPGL has 317 amino acids comprising 4 domains: a cytoplasmic domain from residues 1 to 48, a putative transmembrane domain from residues 49 to 69, an extracellular domain with a stalk region from residues 70 to 157 and an active ligand moiety from residues 158 to 317. OPGL has three known three active fragments consisting of residues 128-316, 137-316, and 158-316 all of which bind and activate osteoclasts *in vitro* (pp. 5 lines 8-26). A fourth fragment of OPGL consisting of residues 75-316 has no biological activity (pp. 5 lines 24-26). OPGL is also known as TRANCE, RANKL, and ODF (osteoclasts differentiation factor) (pp. 5 lines 1-7; see also Figure 2 of Takahashi *et al.* (24 March 1999) "A New Member of Tumor Necrosis Factor Ligand Family, ODF/OPGL/TRANCE/RANKL, Regulates Osteoclast Differentiation and Function." Biochemical and Biophysical Research Communications **256**(3): 449-455).

8. Applicant puts forth the proposition that OPGL and osteoprotegerin act as positive and negative regulators of osteoclasts development and activity, wherein OPGL promotes bone resorption via activation of mature osteoclasts and osteoprotegerin inhibits bone resorption via inhibition of osteoclasts development. This is support by four lines of evidence: (1) injection of mice with recombinant C-terminal domain of OPGL results in severe hypercalcemia (according to Stedman's Medical Dictionary: "An abnormally high concentration of calcium compounds in the circulating blood; commonly used to indicate an elevated concentration of calcium ions in the blood), (2) osteoprotegerin-deficient mice (knock-out mice) develop early onset osteoporosis, (3) mice transgenic for osteoprotegerin develop osteopetrosis, and (4) mice injected with recombinant osteoprotegerin develop osteopetrosis (pp. 7 lines 1-25).

9. The invention encompasses the introduction of immunogenic amino acid sequences (epitopes) into human OPGL (SEQ ID NO: 2) resulting in an immunogenic OPGL construct. This construct is then administered to a mammal such that the endogenous OPGL is immunological suppressed (cleared) resulting in a lower level of OPGL.

10. The Specification also teaches OPGL sequences of SEQ ID NO: 2 for humans and SEQ ID NO: 4 and 6 for mice. Resides 49 to 69 comprising the putative transmembrane domain, residues 70 to 157 comprise the stalk domain, and approximately residues 158 to 316 comprise the active domain. which is representative of mammalian OPGL but does not support non-mammalian animals or non-mammalian OPGL.

11. However, the specification fails to provide any guidance for the successful synthesis, isolation, and characterization of OPGL polypeptides other than mammalian. Further the Specification does not provide adequate guidance as to other non-amino acid based

immunogenic agents may be used (other than epitopes). In addition, the Specification explicitly states that: "As these truncated versions exhibit biological activity, it is logical to direct the autoantibodies against this part of OPGL. In addition, it makes the proteins smaller and thus easier to handle." (pp. 54 lines 10-17)

12. Since the resolution of the various complications in regards to targeting the effect of mutations in a protein, the immunological effect of mutation, the effects of the modified polypeptide in an animal, the isolation and characterization of non-mammalian OPGL, and the immune response to as of yet described non-mammalian OPGL and non-amino acid based immunogenic moieties are highly unpredictable, one of skill in the art would have been unable to practice the invention without engaging in undue trial and error experimentation. In order to practice the invention using the specification and the state of the art as outlined below, the quantity of experimentation required to practice the invention as claimed *in vivo* would require the *de novo* determination of formulations of all the applicable OPGL-epitope combinations. In the absence of any guidance from the specification, the amount of experimentation would be undue, and one would have been unable to practice the invention over the scope claimed.

13. Additionally, a person skilled in the art would recognize that predicting the efficacy of using these ill defined, untested, and hypothesized OPGL-immunogenic constructs *in vivo* based solely on its indirect evidence is highly problematic (see MPEP §2164.02). Furthermore the Applicant states that: "The *in vivo* evidence is partially circumstantial or indirect but is in our opinion..." (pp. 7 lines 3-4), although the specification prophetically considers and discloses general methodologies of using the claimed methods of the undisclosed OPGL-epitope moieties, such a disclosure would not be considered enabling since the state of protein biochemistry and

immunology is highly unpredictable. The factors listed below have been considered in the analysis of enablement [see MPEP §2164.01(a) and *In re Wands*, 858 F.2d 731, 737, 8 USPQ2d 1400, 1404 (Fed. Cir. 1988)]:

(A) The breadth of the claims;
(B) The nature of the invention;
(C) The state of the prior art;
(D) The level of one of ordinary skill;
(E) The level of predictability in the art;
(F) The amount of direction provided by the inventor;
(G) The existence of working examples; and
(H) The quantity of experimentation needed to make or use the invention based on the content of the disclosure.

14. The following references are cited herein to illustrate the state of the art of osteoporosis and immunology.

15. On the nature of the invention, US 6,645,500 B1 (11 November 2003) Halkier & Haaning teaches a similar invention wherein a T cell epitope is inserted into OPGL but US 6,645,500, unlike the instant claims, specifies the position of insertion. This is crucial to the success of the method because the skilled artisan readily recognizes that protein chemistry is an unpredictable area of biotechnology. Proteins with deletion, insertion or substitution/replacement of single amino acid residues may lead to both structural and functional changes in biological activity and immunological recognition, see in particular Skolnick & Fetrow (2000) "From genes to protein structure and function: novel applications of computational approaches in the genomic era." Trends in Biotech. **18**(1): 34-39. For example, Jobling & Holmes (1991) "Analysis of structure and function of the B Subunit of cholera toxin by the use of site-directed mutagenesis." Molecular Microbiology **5**(7): 1755-67 teaches a panel of single amino acid substitutions by oligonucleotide directed mutagenesis which produce

proteins that differ in native conformation, immunological recognition, binding and toxicity. The skilled artisan further recognizes that immunological responses may depend upon the structural characteristics (conformation) of the particular protein (amino acid sequence) targeted. Thus, both biological function and immunological recognition are unpredictable properties which must be experimentally determined. Further it is noted, that for particularly small peptides, conjugation appears to be required for promoting an effective immune response.

16. On the level of predictability in the art, Greenfield *et al.* (1999) "Regulation of Osteoclast Activity." Life Sciences **65**(11): 1087-1102 teaches that the balance between bone formation and resorption is the result of a complex interaction of indirect and direct inhibitors and activators. As little as a 20% increase in bone resorption can lead to the debilitating effects of osteoporosis (pp. 1087; Table 1). As discussed above, perturbation of this balance can have undesired and unpredictable effects. Absent concrete guidance on the structure and position of epitope placement in OPGL and the ensuing immune response, the skilled artisan is confronted with an unpredictable endeavor to fulfill the claims to the full extent of the possible OPGL-epitope combinations.

17. On the state of the prior art, Tsukii *et al.* (19 May 1998) "Osteoclast Differentiation Factor Mediates an Essential Signal for Bone Resorption Induced by 1α,25-Dihydroxyvitamin D_3, Prostaglandin E_2, or Parathyroid Hormone in the Microenvironment of Bone." Biochemical and Biophysical Research Communications **246**(2): 337-341 teaches that administration of rabbit anti-ODF polyclonal antibodies in a fetal long bone culture experiment blocks ODF (also known as OPGL herein) activity (Figure 2). While this lends credence to the invention in concept, it does not offer guidance on how to replicate similar results *in vivo* via active immunization

wherein the animal's immune system down regulates endogenous OPGL. Further, Goldsby *et al.* (2002) Kuby Immunology Chapter 18 "Vaccines" (pp. 449-465) teaches that active immunization is not predictable as peptides are not generally immunogenic.

18. Furthermore, the art is silent as to the existence, isolation, and characterization of non-mammalian orthologues and homologues of OPGL. Thus the skilled artisan is left with no guidance other than the human and murine sequences present in the Specification.

19. Applicant traversed the rejection of the claims on the following grounds: **(a)** a person of ordinary skill in the art would reasonably believe that administering the claimed modified OPGL polypeptides would produce the intended results, **(b)** the Specification provides sufficient guidance, and **(c)** the Declaration of Dr. Hertz under 1.132 filed 12 August 2003 teaches how to make and use the full scope of the invention.

20. Applicant's arguments have been taken into consideration and are not found persuasive for the following reasons.

21. On "**(a)**", enablement is a question of fact not belief. The Examiner has taken the following factors into consideration: the breadth of the claims, the nature of the invention; the state of the prior art, the level of one of ordinary skill, the level of predictability in the art, the amount of direction provided by the inventor, the existence of working examples, and the quantity of experimentation needed to make or use the invention based on the content of the disclosure. The beliefs of the skilled artisan are not taken into consideration.

22. Upon review of the Specification as filed and the prior art, the Examiner has set forth a more applicable rejection of the invention as claimed. The issue at heart of the instant rejection is that the Specification fails to provide guidance for non-mammalian OPGL, non-amino acid

based antigens, and OPGL polypeptides which lack the active domain. In addition, concerning the requirement of the active domain of OPGL (roughly residues 158-316) the Specification explicitly states that: "As these truncated versions exhibit biological activity, it is logical to direct the autoantibodies against this part of OPGL. In addition, it makes the proteins smaller and thus easier to handle." (pp. 54 lines 10-17)

23. On "**(b)**", while immunological OPGL conjugates which stimulate down-regulation of OPGL may constitute a fecund ground for investigation, the CAFC ruled in *Genentech Inc. v. Novo Nordisk A/S* (CA FC) **42 USPQ2d 1001** (1997) that patent protection is granted in return for an enabling disclosure of an invention, not for vague intimations of general ideas that may or may not be workable. Citing *Brenner v. Manson,* **383 U.S. 519, 536, 148 USPQ 689, 696** (1966) (stating, in context of the utility requirement, that "a patent is not a hunting license. It is not a reward for the search, but compensation for its successful conclusion."). Therefore the CFAC stated that tossing out the mere germ of an idea does not constitute enabling disclosure. While every aspect of a generic claim certainly need not have been carried out by an inventor, or exemplified in the specification, reasonable detail must be provided in order to enable members of the public to understand and carry out the invention. That requirement has not been met in the instant specification with respect to the any OPGL conjugates other than those outlined in the scope above which in turns has the desired therapeutic activity.

24. On "**(c)**", the Declaration of Dr. Hertz filed in the instant Application on 12 August 2003 provides guidance on how to make and use the OPGL conjugate as claimed in Application 09/396937 which matured in U.S. 6,645,500. As is readily evident from claim 1 of US '500, the

Declaration was sufficient to support an embodiment of the invention as instantly claimed but not the full breadth of the claims.

25. Thus the specification of the instant application fails to provide adequate guidance for one of skill in the art to overcome the unpredictability and challenges of applying results from *suggestion* and *indirect evidence* to extent the claimed method beyond what is disclosed as exemplified in the references herein.

26. Claims **1, 3, 5, 8-12, 17-24, 28,** and **57-60** are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

27. To provide adequate written description and evidence of possession of a claimed genus, the specification must provide sufficient distinguishing identifying characteristics of the genus. The factors to be considered include disclosure of complete or partial structure, physical and/or chemical properties, functional characteristics, structure/function correlation, methods of making the claimed product, and any combination thereof. In this case, the only factor present in the claim that is sufficiently disclosed is a recitation of mammalian OPGL which approximately comprises residues 158-316 of OPGL. The specification does not identify any particular portion of the structure that must be conserved, a disclosure of structure/function correlation, or provide any examples of non-mammalian OPGL. Nor does the Specification teach any active OPGL fragments which lack the so identified "active domain" approximately comprising 158-316 of

OPGL. The distinguishing characteristics of the claimed genus are not described. Accordingly, the specification does not provide adequate written description of the claimed genus.

28. To satisfy the written-description requirement, the specification must describe every element of the claimed invention in sufficient detail so that one of ordinary skill in the art would recognize that the inventor possessed the claimed invention at the time of filing. *Vas-Cath*, 935 F.3d at 1563; see also *Lockwood v. American Airlines, Inc.*, 107 F.3d 1565, 1572 [41 USPQ2d 1961] (Fed. Cir. 1997) (patent specification must describe an invention and do so in sufficient detail that one skilled in the art can clearly conclude that "the inventor invented the claimed invention"); *In re Gosteli*, 872 F.2d 1008, 1012 [10 USPQ2d 1614] (Fed. Cir. 1989) ("the description must clearly allow persons of ordinary skill in the art to recognize that [the inventor] invented what is claimed"). Thus, an applicant complies with the written-description requirement "by describing the invention, with all its claimed limitations, not that which makes it obvious," and by using "such descriptive means as words, structures, figures, diagrams, formulas, etc., that set forth the claimed invention." *Lockwood*, 107 F.3d at 1572.

29. See *University of Rochester v. G.D. Searle & Co.*, 68 USPQ2d 1424 (DC WNY 2003) and *University of Rochester v. G.D. Searle & Co. et al.* CAFC [(03-1304) 13 February 2004]. In *University of Rochester v. G.D. Searle & Co.* a patent directed to method for inhibiting prostaglandin synthesis in human host using an unspecified compound, in order to relieve pain without side effect of stomach irritation, did not satisfy written description requirement of 35 U.S.C. §112, since the patent described the compound's desired function of reducing activity of the enzyme PGHS-2 without adversely affecting PGHS-1 enzyme activity, but did not identify said compound, since invention consists of performing "assays" to screen compounds in order to

discover those with desired effect. The patent did not name even one compound that assays would identify as suitable for practice of invention, or provide information such that one skilled in art could identify suitable compound. And since specification did not indicate that compounds are available in public depository, the claimed treatment method cannot be practiced without compound. Thus the inventors cannot be said to have "possessed" claimed invention without knowing of a compound or method certain to produce compound. Thus said patent constituted an invitation to experiment to first identify, then characterize, and then use a therapeutic a class of compound defined only by their desired properties.

30. Applicant traversed the rejection of the claims on the following grounds: **(a)** the Specification provides written description for the claimed genus of all modified OPGL polypeptides having preserved B-cell epitopes, **(b)** *University of Rochester v. G.D. Searle & Co.* is not applicable, and **(c)** Applicants are not required to provide a comprehensive list of each and every member of a claimed genus.

31. Applicant's arguments have been taken into consideration and are not found persuasive for the following reasons.

32. On "**(a)**", MPEP §2145 clearly states that attorney argument is not evidence unless it is an admission, in which case, an examiner may use the admission in making a rejection (MPEP § 2129 and §2144.03). Furthermore, the arguments of counsel cannot take the place of evidence in the record. In the instant case the Applicant is asserting that the Specification demonstrates possession of "the claimed genus" while no data, information, or teaching supports the entire genus. The instant Specification provides support for a smaller group with the following defining characteristics: mammalian OPGL comprising the active domain thereof (approximately residues

158-316) and antigenic amino acid sequences {see *In re Schulze*, 346 F.2d 600, 602, 145 USPQ 716, 718 (CCPA 1965); *In re Geisler*, 116 F.3d 1465, 43 USPQ2d 1362 (Fed. Cir. 1997) ("An assertion of what seems to follow from common experience is just attorney argument and not the kind of factual evidence that is required to rebut a prima facie case of obviousness.") and MPEP § 716.01(c)}.

33. On "**(b)**", to the contrary *University of Rochester v. G.D. Searle & Co.* well encompasses the instant situation. The instant claimed are drawn to a massive, ill-defined genus with support for only a smaller group of conjugates (as noted above). Application has consistently argued that any and all variants as instantly claimed may be prepared through routine experimentation (see pp. 7-10 of the instant Reply filed 29 October 2004).

34. On "**(c)**", the instant Specification provides support for a group of OPGL conjugates with the following defining characteristics: mammalian OPGL comprising the active domain thereof (approximately residues 158-316) and antigenic amino acid sequences [see MPEP §2163].

35. Therefore the full breadth of the claim fails to meet the written description provision of 35 U.S.C. §112, first paragraph. Applicant is reminded that *Vas-Cath* makes clear that the written description provision of 35 U.S.C. §112 is severable from its enablement provision.

Summary

36. No claims are allowed.

37. **THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Conclusion

Any inquiry concerning this communication or earlier communications from the examiner should be directed to **Christopher James Nichols, Ph.D.** whose telephone number is **(571) 272-0889**. The examiner can normally be reached on Monday through Friday, 8:00 AM to 5:00 PM. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, **Brenda Brumback** can be reached on **(571) 272-0961**.

The fax number for the organization where this application or proceeding is assigned is **703-872-9306**.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see **http://pair-direct.uspto.gov**. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at **866-217-9197** (toll-free).

Elizabeth C. Kemmerer

CJN
January 25, 2005